



Social functioning increase after repetitive transcranial magnetic stimulation (rTMS) in patients with recurrent major depression

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ABSTRACT

Objectives: Investigating the effectiveness of rTMS (repetitive transcranial of magnetic stimulation) on increase social functioning in patients with recurrent major depression. Method: The subjects were randomly divided in to two groups of 32 patients who had depression on the basis of DSM-IV diagnostic criteria, SCID II, Beck scale in a quasi experimental, pretest – posttest design with control group. 20 sessions of rTMS as the independent factor were carried out on the experimental groups and 12 psychotherapy sessions and drugs treatment was used on each group (control & experimental).Both groups were tested according to (Beck ,Hamilton and SASS) to determine the effect of the independent factor(rTMS) on the dependent factors. Data were analyzed by T test. Results: The comparison between pre &post test of Beck and Hamilton scales showed the reduction of signs & symptoms of depression and increase social functioning in participants. Conclusion: The rTMS is effective in the reduction of signs & symptoms of depression and increase social functioning in recurrent major depression.

Keywords: Social functioning, magnetic stimulation, major depression

INTRODUCTION

Major depressive disorder (MDD) is a public health problem that has tremendous personal and social consequences. Estimates are that 20% of Americans have an episode of depression some time during their adult lives. This disorder damages a lot of people's performance [1]. It is ranked first among global causes of disease burden and disability. Depression is associated with significant physical, medical, and psychological disability. Studies have also shown that recurrent and chronic depression is associated with higher rates of health care utilization, morbidity, and all cause mortality. Those with more severe forms of recurrent MDD who do not respond to first and second line treatment show marked persistent psychosocial functional impairment. This impairment is most notable in how patients perceive their emotional wellbeing, social functioning, vitality, and mental health. These physical and psychosocial impairments are a predictor of relapse in the 6 months following treatment response [2].

On the other hand, social functioning have associated with depression, but it can affect both of symptoms and social functioning. Social functioning include individual interactions with their environment , work ability and prosperity in situations such as work, social activities and all communication with parents and families. Daily performance of person who suffering from depression changed in many areas of life such as position, leisure, marriage and family. The findings of a study confirmed that the treatment of this disorder not only depend on release of symptoms such as bad mood, insomnia, no pleasure or appetite but also another items such as improvement in social functioning.

The vast majority of patients with depression have relapse period. Different factors such as social support, conflict, lack of leisure time, undesirable quality in the relations are the reasons for the relapse. Social dysfunction can lead to negative outcome of treatment and ultimately could even exclude the patient from the social fields or increase relapse rate [3].

Most patients with MDD respond promptly to antidepressant medications, but a significant number fail multiple medication trials. Many of these patients with medication-resistant MDD are treated successfully with electroconvulsive therapy (ECT).

Over the past decade, repetitive transcranial magnetic stimulation (rTMS) has been explored for treatment of MDD. rTMS is a noninvasive procedure involving the application of electrical current pulses, induced by a strong pulsating electromagnetic field. The therapeutic efficacy of rTMS is still being investigated and there have been studies that do not support rTMS as a potent treatment of MDD, however, a number of other investigations have demonstrated that rTMS applied to the left prefrontal cortex is associated with decreased depression in patients with MDD [4-8]. The rTMS which is effective in treatment of signs & symptoms of depression of recurrent major depression [9]. In 1831, Michael Faraday discovered that electrical currents can be converted into magnetic fields and vice versa. His principle of mutual induction is the basis of transcranial magnetic stimulation (TMS). In TMS, a bank of capacitors is rapidly discharged into an electric coil to produce a magnetic field pulse. When the coil is placed near the head of a human or animal, the magnetic field penetrates the brain and induces an electric field in the underlying region of the cerebral cortex [10]. An electrical field of sufficient intensity will depolarize cortical neurons, generating action potentials. These then propagate to exert their biological effects. For example, TMS over the left motor cortex causes action potentials that propagate through the corticospinal tract, causing twitches in contralateral skeletal muscles.

This new technology has been used to affect underlying brain tissue at several levels. First, TMS can alter regional activity within the cortex. Positron emission tomography (PET) has revealed changes in cortical metabolism and dose-dependent changes in regional cortical blood flow in response to TMS [11-13]. Such changes are also observed at sites distant from the magnetic stimulus, showing that the effects of TMS propagate to other parts of the brain [12,13]. The connections demonstrated in this manner correspond to known neural pathways in nonhuman primates, suggesting that the propagation of TMS effects occurs by means of existing neural networks [14]. These distant changes are functionally significant. Wassermann *et al.* [15] found that TMS to one primary motor cortex reduces the response of the contralateral motor cortex to magnetic stimuli. Similarly TMS to one brain region can alter neurotransmitter release elsewhere. For example, TMS to the left prefrontal cortex has been shown to increase release of dopamine in the ipsilateral caudate nucleus [16]. Last, TMS might directly alter gene expression patterns. A study of TMS-induced activation of *cfos* expression in the thalamic paraventricular nucleus of rats found that the expression does not depend on the direction of magnetic stimulus *in vivo* or on the integrity of neural circuitry in brain slices [17]. These findings suggest that magnetic stimulation might alter gene expression directly by a mechanism not dependent on the generation of action potentials.

Repetitive transcranial magnetic stimulation (rTMS) was administered using a high speed stimulator with a figure-eight coil. The left prefrontal cortex rTMS stimulation site was determined by measuring 5cm anterior from motor cortex area [15].

MATERIALS AND METHODS

32 patients between 20-50 years of age meeting DSM-IV-TR criteria of major depression (MDD) with the scores of 20 or greater by Beck Depression Inventory II test (BDI II) were included. They were divided into two groups (control group & experimental group) randomly. All participants were assessed at baseline and after treatment with Hamilton (HAM-D 17) and Social Adaptation Self-evaluation Scale (SASS). It is a 21-item newly developed scale for the evaluation of patient social motivation and behavior in depression. The exclusion criteria were as follows: previous seizures or neurosurgery; any metallic object in brain or skull, patients having pacemakers or hearing aids; any electroconvulsive therapy in the previous 30 days; having pregnant women or having psychosis or the history of bipolar disorder.

Experimental group was under usual treatment (fixed drugs and psychotherapy) and during 20 sessions (5 sessions in week) was under rTMS in left dorsolateral prefrontal cortex (DLPFC), whereas control group gave usual treatments.

Instrument

1) Beck's Depression Inventory 2 (BDI-II) :Beck's Depression Inventory-2 is a 21-item inventory and is one of the most important self-report instruments to measure depression. The inventory has good validity and reliability [18]. Validity and reliability of the inventory in Iran are measured in a study. Cronbach alpha of the inventory is equal to 0.91 and its reliability is reported to 0.96 using retest method [19].

2) Hamilton Scale (HAM) : This scale, has 17 items that measures behavioral, physical and mental symptoms for depression. in 1986 Mehryar and Mosavinasab translate the questionnaire to Persian and prepare it for using. In previous studies reliability assessment via the correlation coefficient was reported between 0.90 and 0.94 by Hamilton. Validity of this scale through solidarity with other tools from 0.60 to 0.84 and internal assessment validity were from 0.84 to 0.90.

3) Structured Clinical Interview for DSM-IV Axis I & II (SCID): SCID is a structured diagnostic measure that is designed to assess DSM-IV Axis I and II disorders. In previous studies, the SCID has demonstrated good reliability [18]. Inter-rater reliability coefficients ranged from 0.48 to 0.98 for categorical diagnosis, and from 0.90 to 0.98 for dimensional assessments (Intra-class correlation coefficient). Internal consistency coefficients have been reported satisfactory 0.71–0.94 [19].The number of criteria must be coded as present and clinically significant in order to obtain an Axis I and II diagnosis threshold. The Persian version of SCID which was employed in this study has satisfactory psychometric properties [20].

4) Social Adaptation Self-Evaluation Scale (SASS): SASS is a 21-item scale in five fields about job, relation with family and friends, Interests and leisure, social attitudes and ability to give management and control of the environment developed for the evaluation of patients' social functioning by Bosc et al. [1]. Levels of social functioning were also objectively evaluated with Global Assessment of Functioning (GAF) scale by a trained psychiatrist. The Cronbach's alpha of Iranian version of this test is equal to 0.701 and the reliability and validity of the Iranian version have been confirmed [3].

5) TMS: Repetitive transcranial magnetic stimulation (rTMS) was administered using a high speed stimulator with a figured eight coil.The left prefrontal cortex rTMS stimulation site was determined by measuring 5cm anterior from motor cortex area. In this study thirty daily rTMS treatments (from Saturday to Thursday in 20 minutes) were administered over the left prefrontal cortex at 90 % of at 20 Hz with 2.5 sec train and 10 sec intertrain [15].

RESULTS

The mean age of the control and experimental groups were 30/93,34/43 respectively. 14 persons of the control group and 5 persons of the experimental group were male and 2 persons of the control group and 11persons of experimental group were female.Statistical analysis of the effect of each treatment methods (medication and psychotherapy) in control group and (medication, psychotherapy and rTMS) in experimental group were analyzed separately, the results of them are presented in below tables.

Table1. Compare the mean of tests scores in the control group on depression scales

Test	Mean-pre	Mean-post	SD	t	df	Sig.
Beck	22.68±4.70	16.87±5.61	4.06	4.11	15	0.001
Hamilton	20.93±3.56	19±3.30	1.69	4.58	15	0.001
SASS	19.06	22.43	3.20	- 4.21	15	0.001

Table 2. Compare the mean of tests scores in the experimental group on depression scales

Test	Mean-pre	Mean-post	SD	t	df	Sig.
Beck	34.6±9.35	15.81±13.21	13.15	5.54	15	0.001
Hamilton	24.93±7.67	11.25±4.73	6.67	8.29	15	0.001
SASS	20.83	35.06	6.67	- 8.53	15	0.001

The above tables show the post tests mean of the Beck Depression Inventory and Hamilton in both the experimental and control groups,that were reduced significantly compare to pre-test.(BDI :T=5.54, P<0.001 and T=4.11, P<0.001) (HAM: T= 8.29 ,P<0.001 and 4.58, P<0.001) . In SASS scale increased significantly in both groups (Exp. T= - 8.53, P<0.001 and Con. T= - 4.21, P<0.001).

DISCUSSION

Depression imposes many economical pressures on developing societies and different ways are intended to treat it. But due to resistance to existing therapies in the researches theTMS could be used as a supplementary therapies [5].

On the other hand social functioning have association with depression [3]. The aim of this study was to determine the antidepressants effect of this technique on symptoms and also social functioning of patients with major depression.

The results reported here support and extend our understanding of the efficacy profile of TMS in the treatment of major depression [21-22], and in this study demonstrate that after 4 weeks (20 sessions) of treatment, there was a statistically significant improvement in patient-reported social function status on the SSAS scale as the improvement on the BDI II & Hamilton scales were predominantly evident in the domains of reduction of sign & symptom of depression. Despite the treatment as usual was effective and significant but in comparison with the means of two groups we understand that TMS therapy is more effective than it.

CONCLUSION

This study has contributed to the growing literature showing that TMS is a safe and effective treatment for patients with major depression as increase social functioning who have failed to receive adequate benefit from treatment as usual (prior pharmacotherapy or psychotherapy). In the other words we have shown that TMS treatment resulted in an improvement in BDI-II and Hamilton as improvements in SASS scale were demonstrated in a population of patients who manifested clinical characteristics reflecting a significant level of treatment resistance and disability due to depression.

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